

CLAIMS

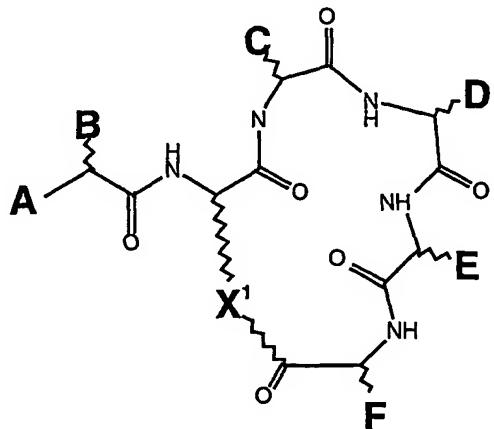
1. A method of treatment of a hypersensitivity condition, comprising the step of administering an effective amount of an inhibitor of a G protein-coupled receptor to a subject in need of such treatment.

5 2. A method according to claim 1, in which the inhibitor is a compound which

(a) is an antagonist of a G protein-coupled receptor,

10 (b) has substantially no agonist activity, and

(c) is a cyclic peptide or peptidomimetic compound of formula I



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where A is H, alkyl, aryl, NH₂, NH-alkyl, N(alkyl)₂, NH-aryl, NH-acyl, NH-benzoyl, NHSO₃, NHSO₂-alkyl, NHSO₂-aryl, OH, O-alkyl, or O-aryl;

20 B is an alkyl, aryl, phenyl, benzyl, naphthyl or indole group, or the side chain of a D- or L-amino acid, but is not the side chain of glycine, D-phenylalanine, L-homophenylalanine, L-tryptophan, L-homotryptophan, L-tyrosine, or L-homotyrosine;

25 C is the side chain of a D-, L- or homo-amino acid, but is not the side chain of isoleucine, phenylalanine, or cyclohexylalanine;

D is the side chain of a neutral D-amino acid, but is not the side chain of glycine or D-alanine, a bulky

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planar side chain, or a bulky charged side chain;

E is a bulky substituent, but is not the side chain of D-tryptophan, L-N-methyltryptophan, L-homophenylalanine, L-2-naphthyl L-tetrahydroisoquinoline, 5 L-cyclohexylalanine, D-leucine, L-fluorenylalanine, or L-histidine;

F is the side chain of L-arginine, L-homoarginine, L-citrulline, or L-canavanine, or a bioisostere thereof; and

10 X is $-(CH_2)_nNH-$ or $(CH_2)_n-S-$, where n is an integer of from 1 to 4; $-(CH_2)_2O-$; $-(CH_2)_3O-$; $-(CH_2)_3-$; $-(CH_2)_4-$; $-CH_2COCHRNH-$; or $-CH_2-CHCOCHRNH-$, where R is the side chain of any common or uncommon amino acid.

3. A method according to claim 2, in which n is 2 or 15 3.

4. A method according to claim 2 or claim 3, in which A is an acetamide group, an aminomethyl group, or a substituted or unsubstituted sulphonamide group.

5. A method according to claim 3, in which A is a 20 substituted sulphonamide, and the substituent is an alkyl chain of 1 to 6 carbon atoms, or a phenyl or toluyl group.

6. A method according to claim 5, in which the substituent is an alkyl chain of 1 to 4 carbon atoms.

7. A method according to any one of claims 2 to 6, 25 in which B is the side chain of L-phenylalanine or L-phenylglycine.

8. A method according to any one of claims 2 to 7, in which C is the side chain of glycine, alanine, leucine, valine, proline, hydroxyproline, or thioproline.

30 9. A method according to any one of claims 2 to 8, in which D is the side chain of D-Leucine, D-homoleucine, D-cyclohexylalanine, D-homocyclohexylalanine, D-valine, D-norleucine, D-homo-norleucine, D-phenylalanine, D-tetrahydroisoquinoline, D-glutamine, D-glutamate, or D-35 tyrosine.

10. A method according to any one of claims 2 to 9, in which E is the side chain of an amino acid selected

from the group consisting of L-phenylalanine, L-tryptophan and L-homotryptophan, or is L-1-naphthyl or L-3-benzothienyl alanine.

11. A method according to any one of claims 1 to 10,
5 in which the inhibitor is a compound which has antagonist activity against C5aR, and has no C5a agonist activity.

12. A method according to any one of claims 1 to 11, in which the inhibitor has potent antagonist activity at sub-micromolar concentrations.

10 13. A method according to any one of claims 1 to 12, in which the compound has a receptor affinity $IC50 < 25\mu M$, and an antagonist potency $IC50 < 1\mu M$.

14. A method according to any one of claims 1 to 13, in which the compound is selected from the group
15 consisting of compounds 1 to 6, 10 to 15, 17, 19, 20, 22, 25, 26, 28, 30, 31, 33 to 37, 39 to 45, 47 to 50, 52 to 58 and 60 to 70 described in PCT/AU02/01427.

15. A method according to claim 14, in which the compound is PMX53 (compound 1), compound 33, compound 60 or compound 45 described in PCT/AU02/01427.

20 16. A method according to any one of claims 1 to 15, in which the inhibitor is used in conjunction with one or more other agents for the treatment of inflammatory bowel disease.

25 17. A method according to claim 16, in which the other agent is infliximab or is an inhibitor of C3a.

18. A method according to any one of claims 1 to 17, in which the treatment is to prevent or alleviate acute recurrences of a hypersensitivity condition.

30 19. A method according to any one of claims 1 to 17, in which the treatment is to prevent or alleviate a primary occurrence of a hypersensitivity condition.

20. A method according to any one of claims 1 to 19, in which the hypersensitivity condition is selected from
35 the group consisting of Type II immediate hypersensitivity (cytotoxic) and Type III (complex-mediated) immediate hypersensitivity, asthma, eczema, dermatitis, Arthus-type

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reactions, glomerulonephritis, hypereosinophilia syndrome, and farmer's lung.

21. A method according to claim 20, in which the hypersensitivity condition is eczema or dermatitis.
- 5 22. A method according to claim 21, in which the hypersensitivity condition is demodectic mange or flea allergy.
23. A method according to claim 21, in which the inhibitor is administered orally or topically.
- 10 24. A method according to claim 20, in which the hypersensitivity condition is asthma.
25. A method according to claim 23, in which the inhibitor is administered orally, intranasally or by inhalation.
- 15 26. A method according to any one of claims 1 to 24, in which the inhibitor is used in conjunction with one or more other agents for the treatment of hypersensitivity conditions.
27. Use of a compound as defined in any one of claims 1 to 15 in the manufacture of a medicament for the treatment of a hypersensitivity condition.